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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
New Jersey District Office

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

March 18, 2003

File #: 03-NWJ-04

Mr. Roger Boissonneault
Chief Executive Officer
Warner Chilcott, Inc.
100 Enterprise Drive, Suite 280
Rockaway, NJ 07866

Dear Mr. Boissonneault:

During the period from October 7, 2002 through October 18, 2002, Investigators Erin McCaffery and Helen Ricalde from our New Jersey District Office conducted an inspection of your firm, located at the above address, to determine your firm's compliance with the Postmarketing Adverse Drug Experience (PADE) reporting requirements of Section 505(k) of the Federal Food, Drug, and Cosmetic Act ("the Act"), and Title 21, *Code of Federal Regulations* ("21 CFR"), Part 314.80.

Based on our review of the inspection report, we conclude that your firm violated Section 301(e) of the Act because it failed to comply with 21 CFR 314.80 and Section 505(k)(1) of the Act. Section 505(k)(1) and 21 CFR 314.80 require an applicant to establish and maintain records, and report data relating to clinical experience and other data or information for drugs for which an approved application is in effect.

Deviations from 21 CFR 314.80 include the following:

1. Failure to review and submit to the FDA adverse drug experience reports as required by 21 CFR 314.80(b) and (c). Specifically, there were twenty-one telephone log entries to your firm describing adverse drug events that were not reviewed or reported to the FDA. These calls include, but are not limited to:

Date of Phone Report	Product Name	Nature of Inquiry**
7/25/02	Estrace tablets	Hair loss
7/10/02	Ovcon 35	Rash
6/24/02	Estrace Cream	Swollen lymph glands
6/6/02	Pyridium	Feeling ill
4/30/02	Ovcon-35	Hives and swelling
4/29/02	Estrace	Extreme constipation
3/19/02	Estrace Cream	Possible vision changes
3/15/02	Doryx	Severe nausea and vomiting
2/20/02	Estrace	Breast tenderness/leg cramps
2/8/02	Estrace	Thyroid problem

** Words/phrases taken verbatim from Medical/Telephone Reports.

2. Failure to maintain records of all adverse drug experiences, including raw data and any correspondence relating to adverse drug experiences, as required by 21 CFR 314.80 (i). Specifically, there were nine telephone log entry reports that were inadequate in that they were illegible or lacked sufficient text to identify the nature of the call in order to determine if a reportable adverse event had occurred. These reports were as follows:

Date of Phone Report	Product	Nature of Inquiry/Response**
6/20/02	Illegible	Illegible text - "no data analysis"
6/17/02	Duricef	"20 degrees Fahrenheit 14 ours"... "however potential for "Illegible text
Undated	Illegible	No text
6/14/02	Pyridium	No text (attached: guide to phenazopyridine)
5/29/02	Estrace	Only entry is "Question"
5/20/02	No text	No text
5/10/02	Doryx	"Laser procedures...not sufficient data ["]... "krypton laser" No text
4/9/02	Pyridium Plus	"ques...use on"... Illegible text... "basis ... as per patient"
4/4/02	Estrace Tablets	"Doctor called-patient had bad allergic reaction. Contain soy or yam?"..illegible text

** Words/phrases taken verbatim from Medical/Telephone Reports

3. Failure to submit to the FDA serious and unexpected adverse drug experience reports within 15 calendar days of initial receipt of information, as required by 21 CFR 314.80(c)(1). These reports include, but are not limited to:

Product	Mfr. Control No.	Receipt Date	Date Sent to FDA	Days
Duricef	[redacted]	7/29/02	9/5/02	38
Pyridium	[redacted]	7/30/02	9/3/02	35
Duricef	[redacted]	6/16/02	7/15/02	29
Doryx	[redacted]	8/8/02	9/4/02	27
Duricef	[redacted]	6/19/02	7/16/02	27
Doryx	[redacted]	8/16/02	9/11/02	26

4. Failure to develop adequate written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experience to FDA, as required by 21 CFR 314.80 (b). Specifically, Procedure # REG-011, Rev. 0, Handling Adverse Drug Experience Reports for Marketed Drugs, dated March 9, 1998, does not:

   a. Establish procedures for transfer of serious, unlabeled event data from the manufacturing site to the reporting site.
   b. Identify the procedures for reviewing incoming complaints requiring medical, quality, or customer service follow-up.
   c. Include procedures to ensure that postmarketing 15-Day Alert reports are promptly investigated, followup reports submitted within fifteen days of receipt of new information, and records maintained of unsuccessful steps taken to seek additional information.
   d. Reference or provide instructions for completion of the Medical/Telephone Report ("blue sheet").
   e. Provide instructions for use of the Contact Summary sheet/ADE Report Form (i.e. yellow sheet) used to obtain all relevant information for completion of the MedWatch 3500A and CIOMS 1 forms.

Neither the above list of deviations nor the Form FDA 483 "Inspectional Observations," which was presented to, and discussed, with Alvin Howard, Vice President, Regulatory Affairs at the conclusion of the inspection, are intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and its regulations. The FDA expects drug manufacturers to establish reasonable mechanisms to assure that all adverse drug experiences are recorded, evaluated and submitted to the FDA within established timeframes as required under 21 CFR 314.80.

We acknowledge receipt of the November 15, 2002 letter from Alvin Howard, Vice President, Regulatory Affairs, to Douglas Ellsworth, Director, New Jersey District, containing responses to the October 18, 2002 FDA 483, Inspectional Observations, issued to your firm. We want to re-emphasize that we consider your firm's inability to establish and implement adequate standard operating procedures for the handling of adverse drug experiences (ADEs), and your firm's failure to evaluate and submit to FDA reports of ADEs, as very serious problems. Your response referred to general corrections to be implemented within the next 60 days. We would like to see a detailed written plan of corrective actions you will implement, with a specific timetable for their implementation. We also want to know how you will be processing ADE data received before the implementation of these corrective actions, to ensure immediate and adequate follow-up and timely submission of initial and followup reports.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions include but are not limited to seizure and/or injunction. Federal agencies are advised of the issuance of all warning letters about drugs and devices so that they may take this information into account when considering the award of contracts.

We request that you reply in writing within 15 working days of receipt of this letter. Your reply should be sent to the Food and Drug Administration, Center for Drug Evaluation and Research (CDER), 11919 Rockville Pike, Rockville, Maryland, 20852, HFD-330, Attn: Denis Mackey Compliance Officer.

Sincerely,

Douglas I. Ellsworth
District Director
New Jersey District

Enclosure: Form FDA 483 dated October 18, 2002